Wilson Disease

National Digestive Diseases Information Clearinghouse

U.S. Department of Health and Human Services

NATIONAL INSTITUTES OF HEALTH

NIDDK
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

What is Wilson disease?

Wilson disease is a genetic disorder that prevents the body from getting rid of extra copper. A small amount of copper obtained from food is needed to stay healthy, but too much copper is poisonous. In Wilson disease, copper builds up in the liver, brain, eyes, and other organs. Over time, high copper levels can cause life-threatening organ damage.

Who gets Wilson disease?

People who get Wilson disease inherit two abnormal copies of the *ATP7B* gene, one from each parent. Wilson disease carriers, who have only one copy of the abnormal gene, do not have symptoms. Most people with Wilson disease have no known family history of the disease. A person's chances of having Wilson disease increase if one or both parents have it.

About one in 40,000 people get Wilson disease.[1] It equally affects men and women. Symptoms usually appear between ages 5 to 35, but new cases have been reported in people aged 2 to 72 years.

[1]Olivarez M, Caggana M, Pass KA, Ferguson P, Brewer GJ. Estimate of the frequency of Wilson's disease in the US Caucasian population: a mutation analysis approach. *Annals of Human Genetics*. 2001;65:459–463.

What causes Wilson disease?

Wilson disease is caused by a buildup of copper in the body. Normally, copper from the diet is filtered out by the liver and released into bile, which flows out of the body through the gastrointestinal tract. People who have Wilson disease cannot release copper from the liver at a normal rate, due to a mutation of the *ATP7B* gene. When the copper storage capacity of the liver is exceeded, copper is released into the bloodstream and travels to other organs—including the brain, kidneys, and eyes.

What are the symptoms of Wilson disease?

Wilson disease first attacks the liver, the central nervous system, or both.

A buildup of copper in the liver may cause ongoing liver disease. Rarely, acute liver failure occurs; most patients develop signs and symptoms that accompany chronic liver disease, including

- swelling of the liver or spleen
- jaundice, or yellowing of the skin and whites of the eyes
- fluid buildup in the legs or abdomen
- a tendency to bruise easily
- fatigue

A buildup of copper in the central nervous system may result in neurologic symptoms, including

- problems with speech, swallowing, or physical coordination
- tremors or uncontrolled movements
- muscle stiffness
- behavioral changes

Other signs and symptoms of Wilson disease include

- anemia
- low platelet or white blood cell count
- slower blood clotting, measured by a blood test
- high levels of amino acids, protein, uric acid, and carbohydrates in urine
- premature osteoporosis and arthritis

Kayser-Fleischer rings result from a buildup of copper in the eyes and are the most unique sign of Wilson disease. They appear in each eye as a rusty-brown ring around the edge of the iris and in the rim of the cornea. The iris is the colored part of the eye surrounding the pupil. The cornea is the transparent outer membrane that covers the eye.

How is Wilson disease diagnosed?

Wilson disease is diagnosed through a physical examination and laboratory tests.

During the physical examination, a doctor will look for visible signs of Wilson disease. A special light called a slit lamp is used to look for Kayser-Fleischer rings in the eyes. Kayser-Fleischer rings are present in almost all people with Wilson disease who show signs of neurologic damage but are present in only 50 percent of those with signs of liver damage alone.

Laboratory tests measure the amount of copper in the blood, urine, and liver tissue. Most people with Wilson disease will have a lower than normal level of copper in the blood and a lower level of corresponding ceruloplasmin, a protein that carries copper in the bloodstream. In cases of acute liver failure caused by Wilson disease, the level of blood copper is often higher than normal. A 24-hour urine collection will show increased copper in the urine in most patients who display symptoms. A liver biopsy—a procedure that removes a small piece of liver tissue—can show if the liver is retaining too much copper. The analysis of biopsied liver tissue with a microscope detects liver damage, which often shows a pattern unique to Wilson disease.

Genetic testing may help diagnose Wilson disease in some people, particularly those with a family history of the disease.

Wilson disease can be misdiagnosed because it is rare and its symptoms are similar to those of other conditions.

Who should be screened for Wilson disease?

Anyone with unexplained liver disease or neurologic symptoms with evidence of liver disease, such as abnormal liver tests and symptoms of liver disease, should be screened for Wilson disease. People with a family history of Wilson disease, especially those with an affected sibling or parent, should also be screened. A doctor can diagnose Wilson disease before the appearance of symptoms. Early treatment can reduce or even prevent illness.

How is Wilson disease treated?

Wilson disease requires lifelong treatment to reduce and control the amount of copper in the body.

Initial therapy includes the removal of excess copper, a reduction of copper intake, and the treatment of any liver or central nervous system damage.

The drugs d-penicillamine (Cuprimine) and trientine hydrochloride (Syprine) release copper from organs into the bloodstream. Most of the copper is then filtered out by the kidneys and excreted in urine. A potential major side effect of both drugs is that neurologic symptoms can become worse—a possible result of the newly released copper becoming reabsorbed by the central nervous system. About 20 to 30 percent of patients using d-penicillamine will also initially experience other reactions to the medication, including fever, rash, and other drug-related effects on the kidneys and bone marrow. The risk of drug reaction and neurologic worsening appears to be lower with trientine hydrochloride, which should be the first choice for the treatment of all symptomatic patients.

Pregnant women should take a lower dose of d-penicillamine or trientine hydrochloride during pregnancy to reduce the risk of birth defects. A lower dose will also help reduce the risk of slower wound healing if surgical procedures are performed during childbirth.

Zinc, administered as zinc salts such as zinc acetate (Galzin), blocks the digestive tract's absorption of copper from food. Zinc removes copper too slowly to be used alone as an initial therapy for people who already have symptoms, but it is often used in combination with d-penicillamine or trientine hydrochloride. Zinc is safe to use at full dosage during pregnancy.

Maintenance therapy begins when symptoms improve and tests show that copper has been reduced to a safe level. Maintenance therapy typically includes taking zinc and low doses of either d-penicillamine or trientine hydrochloride. Blood and urine should be monitored by a health care provider to ensure treatment is keeping copper at a safe level.

People with Wilson disease should reduce their dietary copper intake. They should not eat shellfish or liver, as these foods may contain high levels of copper. Other foods high in copper—including mushrooms, nuts, and chocolate—should be avoided during initial therapy but, in most cases, may be eaten in moderation during maintenance therapy. People with Wilson disease should have their drinking water checked for copper content and should not take multivitamins that contain copper.

If the disorder is detected early and treated effectively, people with Wilson disease can enjoy good health.

Points to Remember

- Wilson disease prevents the body from getting rid of extra copper.
- Wilson disease first attacks the liver, the central nervous system, or both.
- Anyone with unexplained liver disease or neurologic symptoms with evidence of liver disease should be screened for Wilson disease.
- Wilson disease requires lifelong treatment to reduce and control the amount of copper in the body.
- If the disorder is detected early and treated effectively, people with Wilson disease can enjoy good health.

Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases conducts and supports Wilson disease research.

The U.S. Food and Drug Administration is evaluating a new anti-copper drug called tetrathiomolybdate (Coprexa). A National Institutes of Health-supported clinical trial found tetrathiomolybdate to be as effective as trientine hydrochloride in removing copper but with less risk of worsening neurologic symptoms.

For a complete listing of trials being conducted, visit *www.ClinicalTrials.gov*.

For More Information

Wilson's Disease Association International
1802 Brookside Drive
Wooster, OH 44691
Phone: 1–888–264–1450 or 330–264–1450
Email: info@wilsonsdisease.org
Internet: www.wilsonsdisease.org

American Liver Foundation
75 Maiden Lane, Suite 603
New York, NY 10038–4810
Phone: 1–800–GO–LIVER (465–4837)
or 212–668–1000
Fax: 212–483–8179
Email: info@liverfoundation.org
Internet: www.liverfoundation.org

You may also find additional information about this topic by visiting MedlinePlus at *www.medlineplus.gov*.

This publication may contain information about medications used to treat a health condition. When this publication was prepared, the NIDDK included the most current information available. Occasionally, new information about medication is released. For updates or for questions about any medications, please contact the U.S. Food and Drug Administration at 1–888–INFO–FDA (463–6332), a toll-free call, or visit their website at *www.fda.gov*. Consult your doctor for more information.

The U.S. Government does not endorse or favor any specific commercial product or company. Trade, proprietary, or company names appearing in this document are used only because they are considered necessary in the context of the information provided. If a product is not mentioned, the omission does not mean or imply that the product is unsatisfactory.

National Digestive Diseases Information Clearinghouse

2 Information Way
Bethesda, MD 20892–3570
Phone: 1–800–891–5389
TTY: 1–866–569–1162
Fax: 703–738–4929
Email: nddic@info.niddk.nih.gov
Internet: www.digestive.niddk.nih.gov

The National Digestive Diseases Information Clearinghouse (NDDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health of the U.S. Department of Health and Human Services. Established in 1980, the Clearinghouse provides information about digestive diseases to people with digestive disorders and to their families, health care professionals, and the public. The NDDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about digestive diseases.

Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was reviewed by Michael L. Schilsky, M.D., Yale-New Haven Organ Transplant Center.

This fact sheet is also available at *www.digestive.niddk.nih.gov*.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

NIH Publication No. 09–4684
May 2009